



## A polygenic architecture of medication-use across medical conditions

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*Publication date:*  
2020

*Document Version*  
Publisher's PDF, also known as Version of record

[Link to publication from Aalborg University](#)

*Citation for published version (APA):*  
Rohde, P. D., & Nyegaard, M. (2020). *A polygenic architecture of medication-use across medical conditions*. Poster presented at European Society of Human Genetics.

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# A polygenic architecture of medication-use across medical conditions



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## Research aim

To investigate the genetic architecture and biological mechanisms underlying medication-use in the general population.

Previously, [Wu et al \(2019\)](#) performed a genetic analysis in the UK Biobank on medication-use of 23 medication categories.

Here, we extend on these results by investigating medication-use, defined as the total number of different medications currently being used. We do this by performing a GWAS, heritability estimates and genetic correlation analysis.

## Conclusion

We have shown that the total number of different medications people in the UK Biobank currently use has a polygenic architecture.

We identified 57 independent quantitative trait loci for medication-use, and showed that 14% of the phenotypic variation was explained by common genetic variants.

Medication-use had positive genetic correlation with heart diseases, and was negatively correlated with parents age of death and years in school.

The genetic architecture of medication-use is complex, and is not solely driven by common diseases, as indicated by the strong negative genetic correlation.

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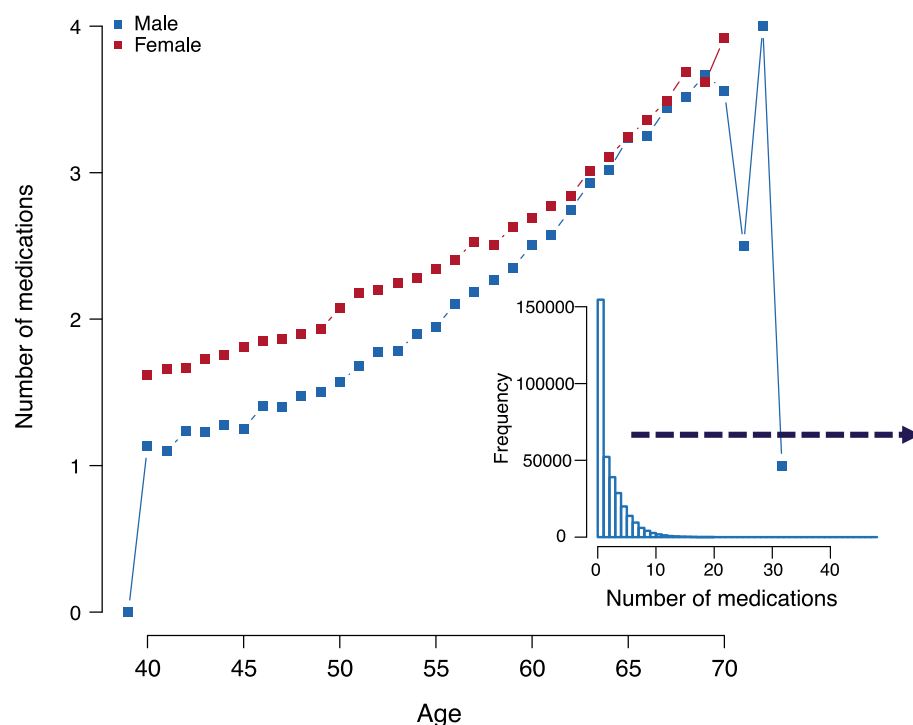


No conflict of interest to declare

## Medication-use

From the UK Biobank we extracted information on medication-use from  $n=335.744$  unrelated white-British individuals (approval ID 31269)

Medication-use was defined as the total number of different medications currently being used by the participants.



## Genetic analysis of medication-use

For the genetic analyses we used ~9 million imputed common genetic variants.

We performed the following analyses:

- Genome-wide association study (by PLINK [\[REF\]](#))
- Genetic correlations (by LD Hub [\[REF\]](#))
- Heritability estimation and partitioning (by SumHer [\[REF\]](#))
- Generic scores (by R-qgg [\[REF\]](#))

3,337 different medications are currently being used.

Top-used drugs (used by 18,000-66,000 individuals) are for;

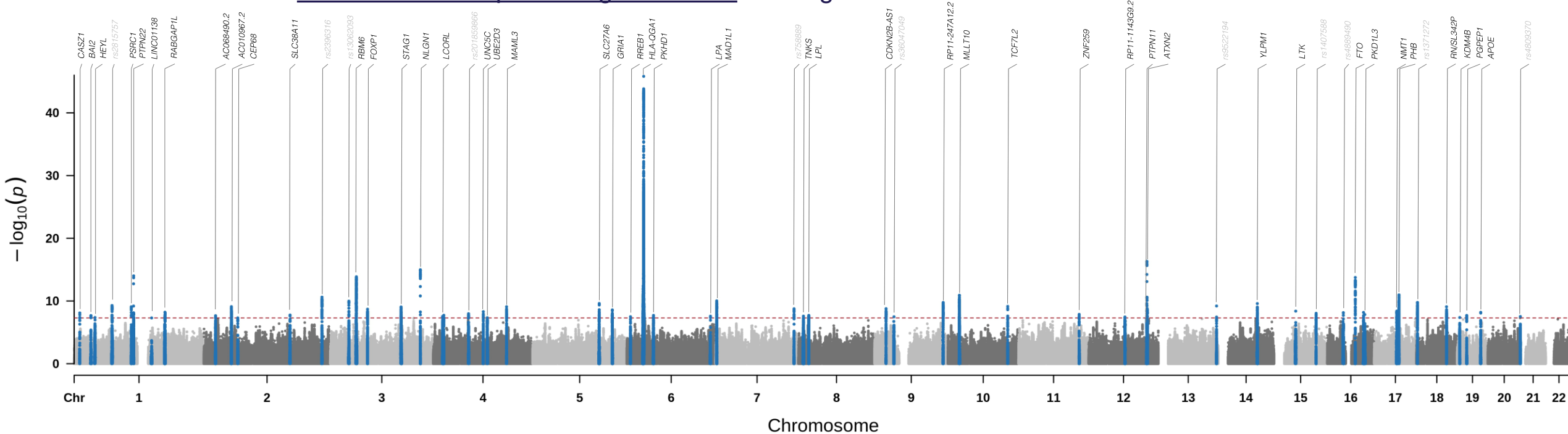
- heart failure and hypertension (ramipril, bendroflumethiazide)
- lowering cholesterol (simvastatin)
- stomach ulcer (omeprazole)
- painkillers and fever lowering (aspirin, ibuprofen, paracetamol)

# RESULTS-I

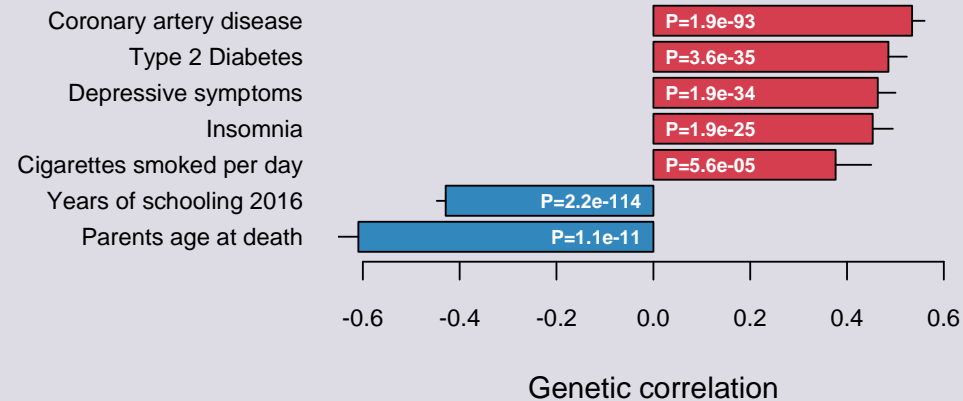


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We identified 57 independent genetic loci showing statistical association with medication-use.



Estimated genetic correlations showed that medication-use was **positively** correlated with common diseases, smoking and depressive symptoms; and was **negatively** correlated with years in school and age of parents death.



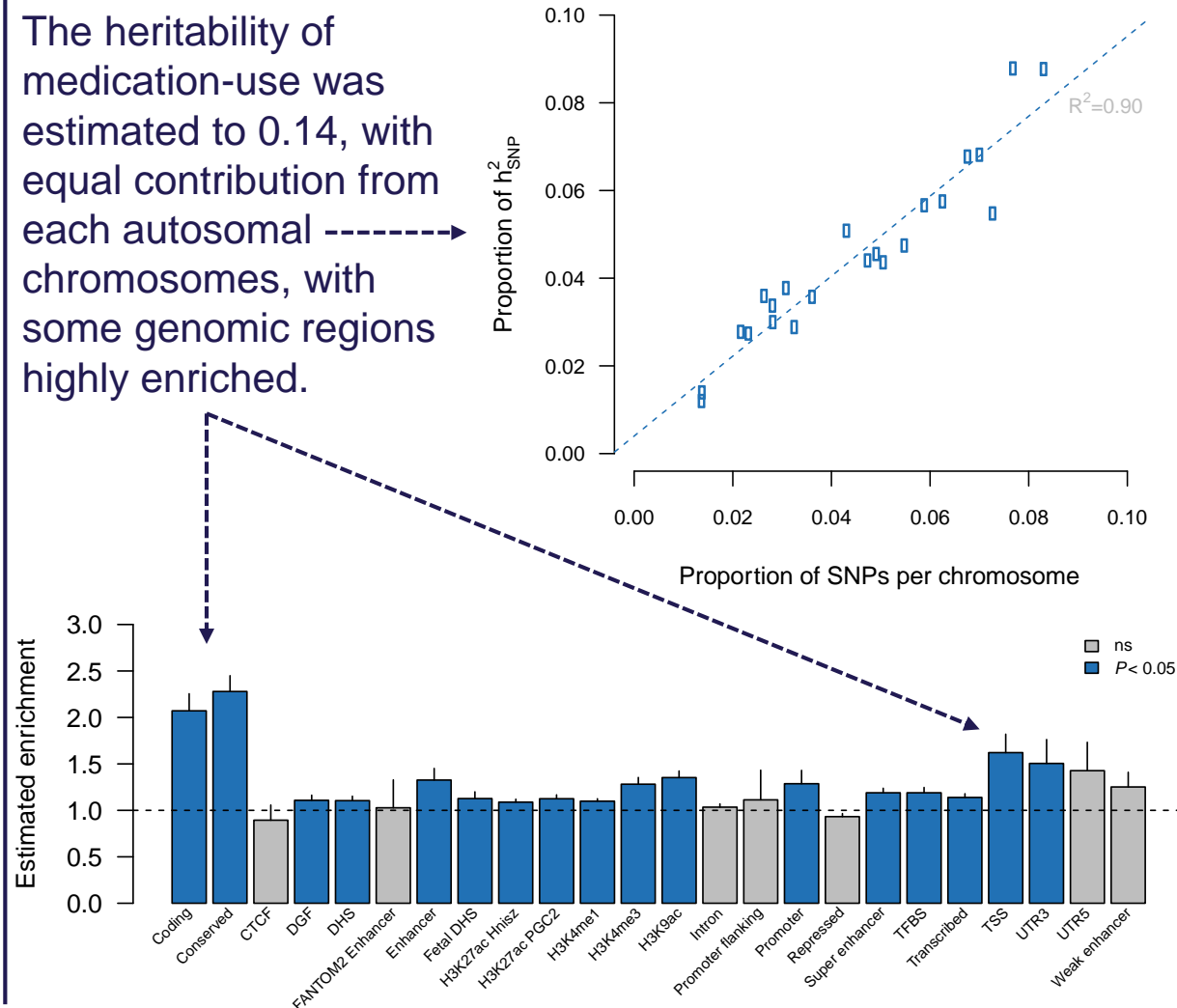
# RESULTS-II



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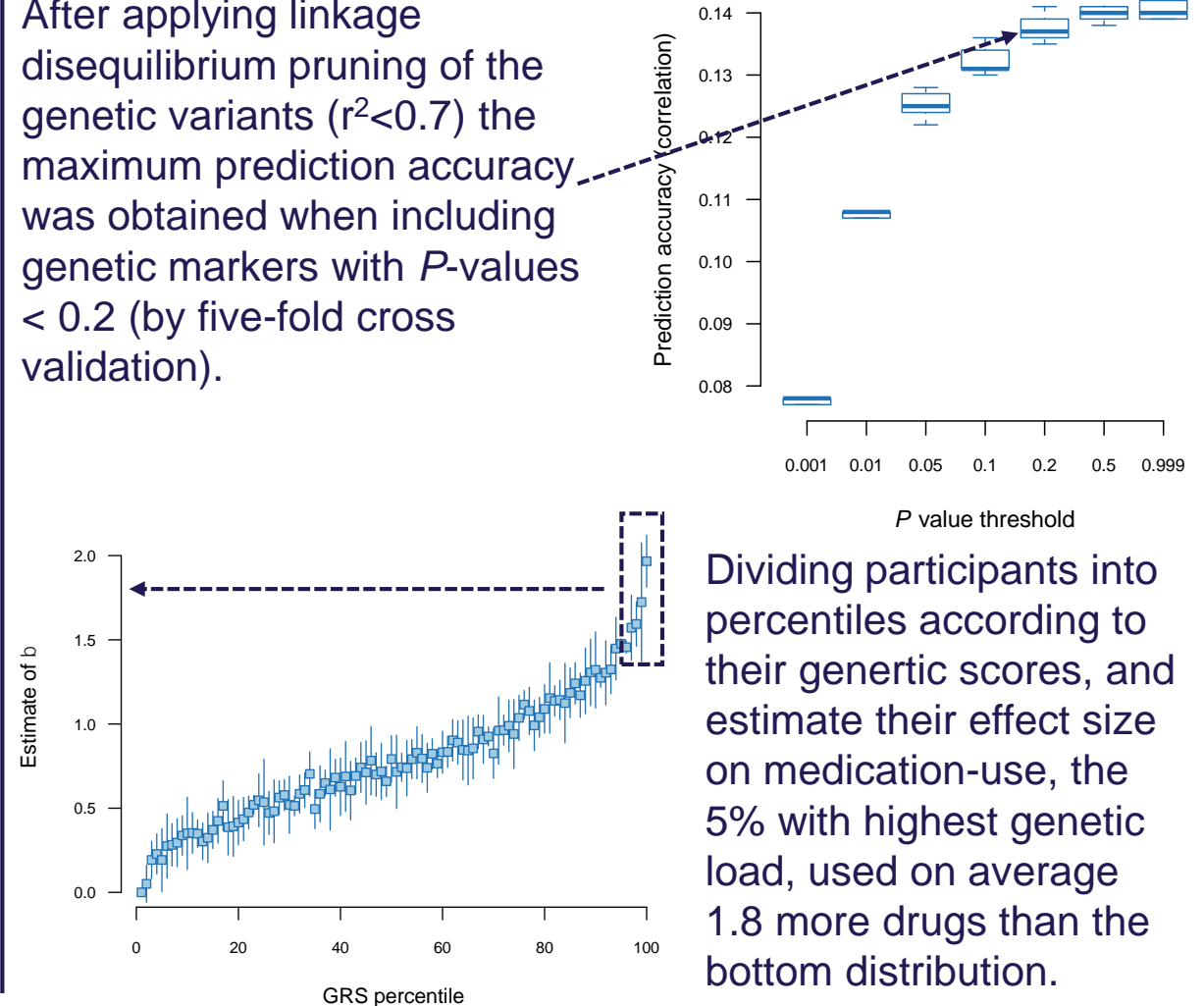
## Decomposing heritability

The heritability of medication-use was estimated to 0.14, with equal contribution from each autosomal chromosome, with some genomic regions highly enriched.



## Predicting medication-use

After applying linkage disequilibrium pruning of the genetic variants ( $r^2 < 0.7$ ) the maximum prediction accuracy was obtained when including genetic markers with  $P$ -values  $< 0.2$  (by five-fold cross validation).



Dividing participants into percentiles according to their genetic scores, and estimate their effect size on medication-use, the 5% with highest genetic load, used on average 1.8 more drugs than the bottom distribution.

# CONCLUSION



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## Study summary

Findings from this study;

- ... 57 independent quantitative trait loci for medication-use.
- ... 14% of the total variation in medication-use in UKBB is explained by common genetic variants.
- ... coding and conserved regions are heavily enriched by genetic variation for medication-use.
- ... positive genetic correlation with heart disease, diabetes, depression, insomnia and smoking.
- ....negative genetic correlated with parents age of death and years in school.
- ... mean prediction accuracy of medication-use was 0.14.
- ... individuals with top 5% genetic load used ~1.8 more drugs than the bottom distribution.

## Perspective

Our results demonstrate that medication-use *per se* is a complex trait irrespectively of medical condition.

The finding that current medication-use was strongly correlated with smoking behaviour, parents age of death, educational level and insomnia, suggest that the genetic architecture of medication-use is not biased towards major common diseases.

Understanding the genetic aetiology of complex diseases has been suggested as the route for improving medical treatment. However, when current medication-use, across medical conditions, appears to have a polygenic architecture, it might be inadequate to solely rely on analyses of complex diseases for improving medical treatment.

Thus, medication-use, or better medication response, is likely to be yet another puzzle piece in understanding complex human diseases, and for providing better medical treatment for future generations.

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